

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Please amend the paragraph starting at page 1, line 32 and ending at page 2, line 12 as follows:

One report has indicated that structures with terminal GlcNAc β 3Gal β 4GlcNAc sequence are present in human ~~leukaemia~~ leukemia cells (Hu et al., 1994). The structures may also be equally present on normal leukocytes. Thus, the relation of the finding to glycosylation patterns generally present in solid tumors was not indicated. This type of saccharide structures may be a part of rare normal glycosylations of human tissues: GlcNAc β 3Gal β 4GlcNAc β 6 sequence linked on O-glycans is probably present on human gastric mucin. A study shows that a monoclonal antibody recognizing GlcNAc β 3Gal β 4GlcNAc β 6 sequence may possibly recognize similar structures on malignant tissues, such as mucinous ovarian neoplasms, pseudopyloric metaplasia of gallbladder and pancreatic epithelia, gastric differentiated carcinoma of stomach, gallbladder and pancreas, and on non-malignant tissues, such as human amniotic fluid, but, however, the structures from ~~malignat~~ malignant tissues were not characterized (Hanisch et al., 1993). The antibody did not recognize neoglycolipid structure GlcNAc β 3Gal β 4GlcNAc β 3Gal β 4 nor carcinomas of lung, colorectum, endometrium or other organs. Another monoclonal antibody raised against testicular cells probably recognizes branched N-acetyllactosamines such as GlcNAc β 3(GlcNAc β 6)Gal β 4GlcNAc- (Symington et al., 1984). Terminal GlcNAc has also been reported from mucins of human foetal mucin (Hounsell et al., 1989). In normal tissues terminal

GlcNAc may be present in minor amounts as biosynthetic intermediates in the biosynthesis of poly-N-acetyllactosamines.

Please amend the paragraph at page 2, lines 28-37 as follows:

Normally there are large amounts of antibodies recognizing terminal GlcNAc structures in human serum. There ~~are~~ is also a class of natural antibodies recognizing terminal Gal α 3Gal β 4GlcNAc- structures. The Gal α antigen is not naturally present in man and recently it was also shown that the natural antibodies bind structures such as GalNAc α 3Gal β 4GlcNAc, GalNAc β 3Gal β 4GlcNAc, and GlcNAc β 3Gal β 4GlcNAc (Teneberg et al., 1996). The X2-structure, GalNAc β 3Gal β 4GlcNAc, is a normal antigen on human tissues and structures GalNAc α 3Gal β 4GlcNAc and Gal α 3Gal β 4GlcNAc have not been described from normal or cancer tissues. Thus, the present finding that the terminal GlcNAc structure is a tumor antigen indicates that the actual function of the natural antibodies might be the prevention of cancers having terminal GlcNAc structures.

Please amend the paragraph at page 3, lines 1-3 as follows:

The following patents describe cancer antigens and their use for making antibodies for ~~therapeutic~~ therapeutic and diagnostic uses and for cancer vaccines. The antigen structures are not related to saccharides of the present invention:

Please amend the paragraph at page 3, lines 14-26 as follows:

In the prior art tumor diagnostic and ~~therapeutic~~ therapeutic antibodies recognizing chitobiose-mannose trisaccharides has been described in DE 38 07 594 A1. The application also

describes other N-glycans with numerous varying terminal structures some of which may comprise also non-reducing terminal N-acetyl glucosamine. Several of the desired structures have been characterized as normal glycans and not cancer specific structures. The application claims to describe structures useful for cancer applications. ~~However~~ However, it is not clear from the invention what the structure of the desired glycan is. Formel (I) may indicate presence of non-reducing terminal GlcNAc, if it is unconventionally read from right to left. However the Formel (I) does not indicate the linkage structure of the terminal GlcNAc. The Formel (III) indicates that the GlcNAc residues are $\alpha 2$, $\alpha 4$, or $\alpha 6$ -linked. The present invention is not directed to such unusual structures. The present invention is directed to human tumor specific ~~glycans comprising~~ glycans comprising non-reducing end terminal β -linked GlcNAc residues.

Please amend the paragraph staring at page 3, line 28 and ending at page 4, line 4 as follows:

Patent application WO 00/21552 claims several unusual O-glycan structures isolated from bovine submaxillary mucin. Two of the structures such as $\text{GlcNAc}\beta 6\text{GalNAc}\alpha 6\text{GalNAc}$ and $\text{GalNAc}\beta 3(\text{GlcNAc}\beta 6)\text{GalNAc}$ comprise terminal GlcNAc-residues. The application did not indicate that said structures would also be related to bovine or human cancers. The present invention is not directed to these structures comprising two GalNAc-residues. The application contains speculation about potential ~~therapheutic~~ therapeutic use of the structures as antigens related to cancer. However, it has not been shown that the structures are related to bovine cancer when these are present in bovine normal submaxillary secretion. Moreover, it is even less probable that the structures would be present in human tissues, the glycosylations are species

specific and vary between human and bovine, e.g. bovine and human glycosyltransferase and glycosylation profiles are different. The human genome is also known and thus glycosyltransferases which could be related to synthesis of the claimed bovine structures should have been now produced and characterized from human. So far none of these has been described in human, or human cancer.

Please amend the paragraph at page 4, lines 19-24 as follows:

Patent application FI20011671 described the general ~~useability~~ usability of terminal GlcNAc-structures in tumor therapy. The application described specific polylactosamine type oligosaccharide sequences containing terminal GlcNAc linked to Gal especially found from glycolipid. The application indicated that the structures can be part of N-linked glycan or O-linked glycans, and that the tumorspecific oligosaccharide sequences can also be linked to O-glycosidic GalNAc. The application did not disclose exact structures of the O-linked or N-linked ~~glycans~~ glycans.

Please amend the paragraph starting at page 4, line 27 and ending at page 5, line 3 as follows:

The present invention describes preferred treatment of cancer when the oligosaccharide sequences have been detected from cancer but not from normal tissues. The present invention is directed to the combination of the analysis and treatment of a cancer. The present application also show for the first time the ~~useability~~ usability of the oligosaccharide sequences of the terminal beta-GlcNAc sequences for cancers of lung, stomach, colon, larynx and mucinous

carcinomas, especially mucinous ovarian carcinomas, forming a group of epithelial type and/or mucin secreting cancers. The present invention is further especially directed to human cancer specific protein linked GlcNAc β -structures. The present invention is also further especially directed to the specified N-glycans and O-glycans and protein linked GlcNAc. The preferred structures form a specific family of terminal specifically "protein linked GlcNAc β -structures" which are human protein linked GlcNAc O-glycans and N-glycans form a specific family of human cancer specific "protein linked GlcNAc β -glycan cores" which are result of defective galactosylation of cancer or tumor tissue.

Please amend the paragraph at page 39, lines 11-26 as follows:

The modified monosaccharides to be used with glycosyltransferases are preferentially nucleotide sugar derivatives or analogs thereof, also other modified glycosides may be transferred by glycosyltransferases. For transglycosylation the modified monosaccharide may be a glycosides like phenyl- or paranitrophenyl-glycoside. The glycosyltransferases are known to tolerate numerous modifications on the donor substrates. Preferentially the nucleotide sugar derivative or analog is derivative of UDP-Gal or UDP-GalNAc where the toxic substance or immunologically active carbohydrate is linked to carbon number 2 or carbon number 6 of the Gal or GalNAc residue or a derivative or analog of UDP-GlcNAc or UDP-Glc where the toxic substance or immunologically active carbohydrate is linked to carbon number 2 or 6 of the Glc or GlcNAc residue or [[or]] a derivative or analog of GDP-Fuc where the toxic substance or immunologically active carbohydrate is linked to carbon number 6 of the fucose residue or, an analog or a derivative of CMP-NeuNAc or CMP-sialic acid where the toxic substance or

immunologically active carbohydrate is linked to carbon number 5, 7, 8, and/or 9 of the NeuNAc or sialic acid residue. Conjugates of NeuNAc and general methods of making nucleotide sugar conjugates have been further described in WO03031464A2.